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**Determinants of the Ambulatory Arterial Stiffness Index Regression Line**  
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# Letter to the Editor

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## Determinants of the Ambulatory Arterial Stiffness Index Regression Line

To the Editor:

Ambulatory arterial stiffness index (AASI) has been proposed as an index of arterial stiffness that can be obtained from 24-hour blood pressure (BP) monitoring without the need for dedicated equipment and personnel.<sup>1</sup> A recent article by Adiyaman et al<sup>2</sup> extends our understanding of AASI by demonstrating that the fit of the regression line of diastolic on systolic BP in individual 24-hour BP recordings (expressed by the coefficient of determination, or  $r^2$ ) has an effect on the relation of AASI with its main clinical and demographic correlates. In a large database, the correlation coefficients of AASI with age, height, 24-hour mean arterial pressure, and 24-hour heart rate were stronger in the subjects with higher coefficients of determination. The authors suggest that AASI might be more meaningful in the subjects with a stronger relation between 24-hour diastolic and systolic BPs and suggest a limitation on future sensitivity analyses to the subjects with an  $r^2$  value of  $>0.36$ .

The question of whether the fit of the regression line of diastolic on systolic BP influences the clinical significance of AASI is of considerable clinical relevance.<sup>1</sup> However, in our view, a more basic question should also be addressed: why does the fit of the regression line vary among the different subjects? It has been observed<sup>3-5</sup> that the strength of the relation between diastolic and systolic BPs might depend in a substantial way on the degree of nocturnal diastolic BP reduction. In other words, subjects with a low coefficient of determination also tend to have a low nocturnal diastolic BP reduction. Of note, this relation is stronger with diastolic than with systolic BP reduction, because diastolic BP is the dependent variable in the regression model used to calculate AASI.

The suggestion by Adiyaman et al<sup>2</sup> to restrict in future sensitivity analyses the use of AASI to those subjects with a higher goodness of fit of the AASI regression line may improve the yield of AASI as a tool for risk stratification in hypertension but has 2 main limitations. First, it would exclude a large subgroup of subjects; second, more importantly, the excluded subjects will mostly have a reduced nocturnal diastolic BP fall (nondippers by diastolic BP). This, in a clinical study, would mean excluding from this interesting analysis those subjects potentially at higher risk. Excluding nondippers circumvents, but does not solve, the problem of the spurious association between AASI and nocturnal diastolic BP reduction.<sup>3</sup> The above association was confirmed by Adiyaman et al<sup>2</sup> in their large database, although it was not uniformly significant in each of the 4

quartiles of the  $r^2$  distribution. This should not come as a surprise, however, given that splitting the study population into quartiles of  $r^2$  reduces to a great extent the variability of nocturnal diastolic BP reduction, which is the strongest determinant of  $r^2$ .<sup>3-5</sup>

The modified AASI based on a symmetrical regression, as suggested by Gavish et al,<sup>4</sup> could be helpful in this regard, by providing an estimate of AASI, which is less affected by the nocturnal BP fall and by the goodness of fit of the regression slope.

## Disclosures

None.

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1. Dolan E, Thijs L, Li Y, Atkins N, McCormack P, McClory S, O'Brien E, Staessen JA, Stanton AV. Ambulatory arterial stiffness index as a predictor of cardiovascular mortality in the Dublin Outcome Study. *Hypertension*. 2006;47:365-370.
2. Adiyaman A, Dechering DG, Boggia J, Li Y, Hansen TW, Kikuya M, Björklund-Bodegård K, Richart T, Thijs L, Torp-Pedersen C, Ohkubo T, Dolan E, Imai Y, Sandoya E, Ibsen H, Wang J, Lind L, O'Brien E, Thien T, Staessen JA; International Database on Ambulatory Blood Pressure Monitoring in Relation to Cardiovascular Outcomes Investigators. Determinants of the ambulatory arterial stiffness index in 7604 subjects from 6 populations. *Hypertension*. 2008;52:1038-1044.
3. Schillaci G, Parati G, Pirro M, Pucci G, Mannarino MR, Sperandini L, Mannarino E. Ambulatory arterial stiffness index is not a specific marker of reduced arterial compliance. *Hypertension*. 2007;49:986-991.
4. Gavish B, Ben-Dov IZ, Bursztyn M. The linear relationship between systolic and diastolic blood pressure monitored over 24 hours: assessment and correlates. *J Hypertens*. 2008;26:199-209.
5. Schillaci G, Parati G. Ambulatory arterial stiffness index: merits and limitations of a simple surrogate measure of arterial compliance. *J Hypertens*. 2008;26:182-185.

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## **Response to Determinants of the Ambulatory Arterial Stiffness Index Regression Line**

Ahmet Adiyaman, Dirk Dechering, Theo Thien, José Boggia, Yan Li, Ji-Guang Wang, Tine W. Hansen, Eoin O'Brien, Tom Richart, Lutgarde Thijs and Jan A. Staessen

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## Response to Determinants of the Ambulatory Arterial Stiffness Index Regression Line

We thank Schillaci and colleagues for their continued interest<sup>1-3</sup> in the ambulatory arterial stiffness index (AASI). Schillaci et al<sup>1</sup> reported that the inverse association between AASI and nocturnal dipping is stronger for diastolic than for systolic blood pressure. This observation has no repercussion on  $r^2$ , which is a measure of fit of the regression line. When A (diastolic blood pressure) is regressed on B (systolic blood pressure) or vice versa, estimates of  $r^2$  are exactly the same.

With regard to the proposed threshold value of  $r^2$  (0.36), Schillaci and colleagues<sup>1-3</sup> might have misunderstood the perspectives of our article.<sup>4</sup> We made the distinction between risk stratification in individual subjects and clinical outcome research in groups. We proposed to apply the 0.36 threshold for individual risk prediction, because for a patient, prognostic accuracy is a key issue. For clinical and epidemiological research in groups, we stated that it is not good practice to exclude subjects from analysis based on an arbitrary threshold. We suggested that the results from a primary analysis involving all of the available subjects be substantiated in a sensitivity analysis, from which subjects would be excluded with an AASI  $r^2$  value  $<0.36$ .<sup>4</sup> The overall analysis on all of the subjects excludes the introduction of bias. The secondary analysis does not exclude a large group, but only a maximum of 20% of subjects.<sup>4</sup>

The last argument of Schillaci et al<sup>3</sup> refers to the so-called "spurious" association between AASI and the nocturnal fall in diastolic blood pressure. We do not consider this inverse association, which in fact was first reported by Schillaci et al<sup>1</sup> and confirmed by us,<sup>4</sup> to be spurious. In statistical terms, a spurious association may arise if the same variables are used to define the dependent and explanatory variables in a regression equation. AASI involves the 24-hour systolic and diastolic blood pressures. The nocturnal blood pressure fall is the difference between the daytime and nighttime ambulatory blood pressures.<sup>5</sup> The qualifier "spurious," in our opinion, does not, therefore, apply to the inverse relation of AASI with the nocturnal fall in either systolic or diastolic blood pressure.

Finally, we did not find a consistent association between  $r^2$  and the nocturnal fall in systolic or diastolic blood pressure. Figure 1<sup>4</sup> of our article illustrates 3 subjects with the same value of AASI (0.50). The nocturnal fall in blood pressure, expressed as a percentage of the daytime level, was 10.5% systolic and 13.1% diastolic in the subject with an  $r^2$  of 0.23. For the subject with an  $r^2$  of 0.45, these percentages were 5.3% and 6.0%, respectively. For the subject with an  $r^2$  of 0.86, these values were 14.4% and 19.9%.

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## Disclosures

None.

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- Schillaci G, Parati G, Pirro M, Pucci G, Mannarino MR, Sperandini L, Mannarino E. Ambulatory arterial stiffness index is not a specific marker of reduced arterial compliance. *Hypertension*. 2007;49:986-991.
- Schillaci G, Parati G. Ambulatory arterial stiffness index: merits and limitations of a simple surrogate measure of arterial compliance. *J Hypertens*. 2008;26:182-185.
- Schillaci G, Pucci G, Mannarino MR, Pirro M, Parati G. Determinants of the ambulatory arterial stiffness index regression line. *Hypertension*. 2009;53:e33.
- Adiyaman A, Dechering DG, Boggia J, Li Y, Hansen TW, Kikuya M, Björklund-Bodegård K, Richart T, Thijs L, Torp-Pedersen C, Ohkubo T, Dolan E, Imai Y, Sandoya E, Ibsen H, Wang J, Lind L, O'Brien E, Thien T, Staessen JA, on behalf of the International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcome (IDACO) investigators. Determinants of the ambulatory arterial stiffness index in 7604 subjects from 6 populations. *Hypertension*. 2008;52:1038-1044.
- Li Y, Wang JG, Dolan E, Gao PJ, Guo HF, Nawrot T, Stanton AV, Zhu DL, O'Brien E, Staessen JA. Ambulatory arterial stiffness index derived from 24-hour ambulatory blood pressure monitoring. *Hypertension*. 2006;47:359-364.